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Award Number: DAMD17-00-1-0659

TITLE: Do the Effects of Exercise on Breast Cancer Vary with
Environment?

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REPORT DATE: October 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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20021231 116

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE October 2002	3. REPORT TYPE AND DATES COVERED Annual (18 Sep 01 -17 Sep 02)	
4. TITLE AND SUBTITLE Do the Effects of Exercise on Breast Cancer Vary with Environment?			5. FUNDING NUMBERS DAMD17-00-1-0659	
6. AUTHOR(S): Jane Teas, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of South Carolina Columbia, South Carolina 29208 Jane.teas@palmettohealth.org			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE	
13. Abstract (Maximum 200 Words) (abstract should contain no proprietary or confidential information) We propose to study 10 healthy postmenopausal women who normally exercise. We will ask these women to have their blood drawn before and after an hour of exercise outdoors on a sunny day and then a week later indoors on a treadmill in a room with only indoor lighting. We propose that exercise done outdoors will have a different effect on vascular endothelial growth factor (VEGF), hypoxia inducible factors 1 α and β , vitamin D activity, and estrogen metabolism as measured by the ratio of 2 hydroxyestrone and 16 α -hydroxyestrone. Elucidation of indoor versus outdoor influences on exercise induced metabolism may be important in understanding variations in reports of the protective nature of exercise on breast cancer prevention.				
14. SUBJECT TERMS breast cancer, exercise, environment			15. NUMBER OF PAGES 11	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

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Do the Effects of Exercise on Breast Cancer Prevention Vary With Environment?

Introduction

During exercise, chemical, neural, and hormonal factors work together to direct blood flow towards the heart and skeletal muscles, and via vasoconstriction, away from areas such as skin, gut, spleen, liver, and kidneys (1). Although no one has documented reduced blood flow to the breasts during moderate exercise, it is likely.

The central concept in this proposal is that exercise, by temporarily reducing blood flow to the breasts, induces a transient state of hypoxia. Exercise is known to induce a temporary state of hypoxia (2). Hypoxia increases vascular endothelial growth factor (VEGF) activity in tumor cells (3); hypoxia-inducible factor 1 alpha (HIF-A) (3) and metastatic potential. However, habitual and/or lifetime exercise is a life-style factor associated with a lower incidence of many forms of cancer.

Sunlight during exercise may also be an important factor. The finding that exercise may provide protection against developing many forms of cancer, including breast cancer is paradoxical to the findings about the effects of hypoxia on tumor cells.

The mechanisms underlying these phenomena and the apparent paradox have not been identified. In an effort to begin to explore this paradox, we hypothesize that exercise-induced hypoxia will decrease susceptibility to or reoccurrence of breast cancer in post-menopausal women, and that sunlight will enhance the effects of exercise on breast cancer prevention. To answer this question, we will do two experiments. Subjects will exercise for one hour outdoors in the sunlight and one hour indoors on a treadmill in the absence of sunlight.

Body of Report

Task 1. Develop Plan for Study Computer Database, Months 1-3

- a. Normal study values will be entered for each outcome variable, so out-of-range values will immediately alert investigators to potential problems.
Since all analyses are being performed at the end of the study, rather than concurrent with the study, and normal values may not be relevant, we are plotting the values longitudinally for each patient to see where an individual's values might have varied.
- b. Access database will be developed to monitor each volunteer and to record data from laboratory analyses and medical histories.
Tracking system is in place.

Task 2. Obtain IRB approval from local institutions (Palmetto Health Alliance and the University of South Carolina).

- a. Done

Task 3. Obtain IRB approval from the U.S. Army

- a. HSRRB met on October 10, 2001 to review the grant.
- b. HSRRB Board members recommended approving this protocol with modifications October 19, 2001.
- c. Modifications were accepted
- d. However, no use of human subjects could begin until arrangements for insurance were made by the University of South Carolina, to be paid by the U.S. Army. A carrier was identified, but so far, no money has been released by the U.S. Army to pay for the insurance.

Task 4. Subject Recruitment and Study, Months 5-7

No recruitment can begin until money is released by the U.S. Army to pay the insurer identified by the University of South Carolina.

Recruitment of healthy volunteers and selection of eligible subjects is estimated to take 3 months.

- a. We will rely on word of mouth to recruit healthy postmenopausal women who regularly exercise and take no medications. This may take several months.
- b. Once 10 subjects have been recruited, we will begin the study.
- c. Study will last 2 weeks for each of the 10 subjects.

Task 5. Data Analysis of Results from Healthy Volunteers, Months 8-12

- a. Meetings with oncologists and member of the Exercise Sciences Department at the University of South Carolina to present preliminary data.
 1. Meetings will take place as soon as the data are available.
- b. Final meeting with volunteers to explain study results and to answer any questions.
 1. Meeting is scheduled for September, by which time all the analyses should be completed.

Key Research Accomplishments

- 1. Narrowed the scope of the research to include only women living at approximately 300 ft (100 meters) in .Columbia, South Carolina.**
- 2. Added Dr. Stephanie Muga as a co-PI**
- 3. Refined the biological endpoints to be used in the study.**
- 4. Received Scientific Review, local IRB review in South Carolina, and Army HSRRB approvals.**
- 5. Identified an insurer acceptable to both the University of South Carolina and the U.S. Army. Awaiting release of funds to pay for insurance before recruitment can begin.**

Reportable Outcomes

None yet. Volunteers will be recruited as soon as permission to begin the study is granted. The begin date is dependant on arrangements between the US Army and the University of South Carolina to pay for insurance.

Conclusions

1. All Human Subjects concerns and Scientific Review concerns have been met.
2. Specific results of the study are not yet available.
3. The U.S. Army and the University of South Carolina are negotiating issues of insurance coverage.

References

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2. Jammes Y, Zattara-Hartmann MC, Badier M. Functional consequences of acute and chronic hypoxia on respiratory and skeletal muscles in mammals. Comparative Biochem & Physiology, Part A. (1997) 118(1):15-22. Sep
3. Ruohola JK, Valve EM, Karkkainen MJ, et al. Vascular endothelial growth factors are differentially regulated by steroid hormones and antiestrogens in breast cancer cells. Molec & Cell Endocrin (1999) 149(1-2):29-40. Mar

Appendices

None yet.

List of Personnel

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